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Scott R. Hansen

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/691,033
Applicant	:	Zongqin Xia, et al.
Filed	:	October 21, 2003
Art Unit	:	1654
Examiner	:	Susan D. Coe
Title	:	SMILAGENIN AND ITS USE
Docket No.:	:	HASEL-65949
Customer No.	:	24201

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

I, Daryl Rees, hereby declare as follows:

1. I hold the degrees of MSc in Pharmacology (London, England, 1985) and PhD in Pharmacology (London, England, 1991). I hold the position of Chief Operating Officer of Phytopharm plc, the Assignee of this patent application. I joined Phytopharm plc in June 1999 from University College, London, England, where I was then a Senior Lecturer in Clinical Pharmacology. I am an Honorary Senior Lecturer in the Department of Medicine at University College, London, a former Editor of the British Journal of Pharmacology, and Chairman of the Huntingdon Research Ethics Committee.

2. The information provided in this Affidavit is taken from the relevant records of Phytopharm plc, to which I have full access, and my personal knowledge.

3. I have studied the Office Action of February 17, 2005 and note that claims 5-8 are rejected as claiming subject matter that was not explained in the specification such that one

skilled in the art could make or use the invention. However, the specification does, indeed, provide an enabling disclosure of the claimed invention.

3. Parkinson's disease is a degenerative brain disorder, probably caused by decreased activity of the neurotransmitter dopamine within the striatum of the basal ganglia. The basal ganglia are a set of structures buried deep within the brain that are involved with the control and sequencing of movement. The striatum is the part of the basal ganglia that receives connections from the motor areas of the cortex that are responsible for organizing movement commands. The striatum also receives connections from the dopamine-producing cells at the base of the brain where it connects to the spinal cord (brainstem). This particular part of the brainstem, which produces dopamine, is known as the substantia nigra. The cells of the substantia nigra connect to the striatum, where they release dopamine. Symptoms usually begin in middle to later life with trembling of the lips and hands, loss of facial expression, and muscular rigidity. As it progresses it may bring on body tremors, particularly in muscles at rest. Movements become slow and difficult; walking degrades to a shuffle. After many years physical incapacity may occur. Dementia occurs in some patients; depression is also common.

4. Measuring the ability of drug candidates to upregulate neuronal receptors at appropriate locations of the cortex and neuromuscular system, so that transmission of relevant signals in the neurons is possibly improved to compensate for the depleted dopamine levels in the Parkinson's patient, is therefore in principle a realistic approach to the treatment of Parkinson's disease.

5. Measuring the ability of drug candidates to enhance general cognitive performance is also in principle a useful approach for assessing candidate drugs for possibly treating neurodegenerative disorders generally, including Parkinson's disease.

6. A combined assessment strategy, using both receptor assays (Examples 1 and 2) and cognitive performance enhancement (Example 3) indicators, is therefore a credible strategy in the case of drug candidates for treating Parkinson's disease.

7. From the data of Examples 1 to 3, and further on the basis of the detailed analysis of prior knowledge of the role of receptors in neurodegenerative diseases, as set out in the Specification, the claimed prediction of activity of smilagenin in treating Parkinson's disease was made. That prediction was inherently reasonable at the time. Further, as set out below, that prediction has been proved to have been accurate.

8. The Assignee has conducted specific trials on cultured primary neuron cells relevant to neurodegenerative disorders, including Parkinson's disease. The results of these tests, and a discussion of them, are attached as Exhibit 1. The tests show that, as predicted in the application, smilagenin shows very good activity on these Parkinson's disease models. The tests also show that the activity on the Parkinson's disease models correlates with the activity shown in the application on the receptor screen in this type of compound (see Table 3 of the application, which predicts activity also in sarsasapogenin and no activity in diosgenin). Thus, the description provided in the Specification was credibly predictive of activity in the treatment of Parkinson's disease, and a person of ordinary skill in the art would be able to determine this effectiveness of smilagenin, without any undue experimentation.

9. Based on the foregoing, the subject matter of claims 5-8 was reasonably described in the specification to such an extent that one skilled in the art could make or use the invention.

I hereby state that the foregoing is true and correct to the best of my knowledge, and that all statements of fact are based on personal knowledge and/or reasonable investigation.

28th June 2005
Dated

Daryl Rees

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